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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,444	09/17/2001	James M. Wilson	UPN-N2605	1285

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	16

DATE MAILED: 06/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/955,444	WILSON ET AL.	
	Examin r	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10-17 and 19* is/are pending in the application.

4a) Of the above claim(s) *8,9,18 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10-17,19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,11,14,15*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Claims 1-22 are pending.

The amendment to claims 10-17 in paper no. 13 has been entered.

Election/Restrictions

Applicant's election with traverse of Group III in Paper No. 13 filed on 4/14/03 is acknowledged. The traversal is on the ground(s) that claim 1 should have been designated a generic claim, and that any restriction requirement should have been made a species restriction among the specified transgenes. This is not found persuasive because the transgenes are not species for the reasons set forth in paper no. 12 filed on 3/12/03. There is not relationship between the transgenes because each transgene is used in a different therapeutic method and does not share a common structure with the other transgenes. In addition, MPEP 808.01 states, "Where there is no disclosure of relationship between species (see MPEP § 806.04(b)), they are independent inventions and election of one invention following a requirement for restriction is mandatory even though applicant disagrees with the examiner".

The requirement is still deemed proper and is therefore made FINAL.

Claims 8, 9, 18, and 20-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13 filed on 4/14/03.

Priority

The statement "This Application is a CIP of PCT/US01/1300 filed on 4/23/01, which claims benefit of US Application No. 60/200,409" on the first line of the specification is acknowledged.

Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: the claims are not supported under 35 U.S.C. 112, first paragraph, as failing to comply with the written description and enablement for the reasons set forth below.

The provisional application does not disclose a non-invasive method of delivering a secreted product to the bloodstream of a mammal by administering the product to the lungs of the mammal.

In addition, the provisional application set forth a list of products that the recombinant AAV can carry and methods of administration known to one skilled in the art. However, nothing in the provisional application would lead one to the particular combination set forth in the claims of application 09/955,444. "It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose." *Lockwood v. American Airlines Inc.,* 41 USPQ2d 1961, 1966 (CAFC 1997).

Claim Objections

Claim 7 is objected to because of the following informalities: there are non-elected inventions in claim 7. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4, 7, 10, 11, 12, 13, 14, 15, and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Li et al. (IDS, US 2001/0036454, EFD 2/17/00). Li teaches a method of a recombinant adeno associated virus (AAV) comprising a transgene to the cells of a lung, wherein the cells express the transgene and the protein is thereby expressed into the circulatory system (abstract). Once entering the circulatory system the protein is able to achieve a systemic therapeutic effect. The method can be used for treating hemophilia and Factor IX can be used in the method (page 3). The AAV has a transgene of interest flanked by AAV ITR sequences (page 7). The cap protein uses the ITR sequences to package the AAV genome into an AAV viral particle. Li teaches that there are three types of pharmaceutical inhalation devices most heavily used (page 10).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 5, 6, 10, 15, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (IDS, US 2001/0036454) taken with either Rabinowitz et al. (US 6,491,907) or Hildinger et al. (Journal of Virology, 75,6199-6203, July 2001).

Li teaches a method of a recombinant adeno associated virus (AAV) comprising a transgene to the cells of a lung, wherein the cells express the transgene and the protein is thereby expressed into the circulatory system (abstract). Once entering the circulatory system the protein is able to achieve a systemic therapeutic effect. The method can be used for treating hemophilia

and Factor IX can be used in the method (page 3). The AAV has a transgene of interest flanked by AAV ITR sequences (page 7). The cap protein uses the ITR sequences to package the AAV genome into an AAV viral particle. Li teaches that there are three types of pharmaceutical inhalation devices most heavily used (page 10). However, Li does not specifically teach using an AAV comprising ITRs of an AAV serotype heterologous to the serotype of the AAV capsid protein in the gene delivery method described above.

However, at the time the invention was made, Rabinowitz teaches making and using recombinant hybrid AAV vectors comprising an AAV genome (ITRs) from AAV2 and an AAV capsid from AAV5 (column 8, lines 4-12) to avoid some of the problems associated with AAV vectors. The prevalence of neutralizing antibodies against AAV-2 within the human population (column 8, line 47-54).

In addition, at the time the invention was made, Hildinger teaches using an adeno-associated virus serotype 2 (ITR and rep) and 5 (Cap) for gene transfer (abstract). Hildinger further teaches the advantages of the AAV2/5 vector is that it should be serogically distinct from AAV2 based on antibody neutralization and greater transduction efficiency compared to AAV 2 (pages 6199-6201).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Li taken with either Rabinowitz or Hildinger to make and use a hybrid AAV vector in the non-invasive gene therapy method. One of ordinary skill in the art would have been motivated to make and use the hybrid AAV vector because of the greater transduction efficiency and no cross-neutralization between AAV2/5 and AAV2.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (IDS, US 2001/0036454) taken with Xiao et al. (IDS, Experimentally Neurology 144, 113-124, 1997).

Li teaches a method of a recombinant adeno associated virus (AAV) comprising a transgene to the cells of a lung, wherein the cells express the transgene and the protein is thereby expressed into the circulatory system (abstract). Once entering the circulatory system the protein is able to achieve a systemic therapeutic effect. The method can be used for treating hemophilia and Factor IX can be used in the method (page 3). The AAV has a transgene of interest flanked by AAV ITR sequences (page 7). The cap protein uses the ITR sequences to package the AAV genome into an AAV viral particle. Li teaches that there are three types of pharmaceutical inhalation devices most heavily used (page 10). However, Li does not specifically teach using AAV at a dose of $1x10^{10}$ to 1×10^{15} in the gene delivery method described above.

However, at the time the invention was made, Xiao teaches gene transfer using AAV and that AAV can be produced at very high titers 10^{12} viral particles/ml (page 113).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Li taken with Xiao to make a dose of AAV at 10^{12} viral particles/ml and used the dose in the non-invasive method. One of ordinary skill in the art would have been motivated to make and use the 10^{12} viral particles/ml dose to improve the transgene expression and because Xiao teaches that AAV can be produced at very high titers.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Conclusion

Hortelano et al. is cited on the PTO-892 to display the state of the art for gene therapy for hemophilia using AAV comprising a Factor VIII gene product.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

Brian Whiteman
Patent Examiner, Group 1635

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER